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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,060	06/13/2005	Rolf Baenteli	TX/4-32366A	8326

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EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
12/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/507,060	BAENTELI ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4 and 7-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4, 7-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the amendment filed on September 5, 2008.

Claims 1-2, 4 and 7-9 are pending in this application.

Withdrawn Rejections/Objections:

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

The following rejections are maintained:

1. Claims 7-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a compound of formula (I) and a method of treating breast tumor comprising the step of administering a compound of formula (I), does not reasonably provide enablement for a composition which comprises (a) a therapeutically effective amount of the compound of formula I and (b) a second drug substance (claim 7); or a method for treating all of the diseases recited in claims 8-9. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The reasons from the previous office action are incorporated here by reference.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. With regards to claim 7, applicant argues that 'the claim has been amended to be

dependent on claim 1 and the scope of the claim is well defined and enabled by the instant application'. This is not, however, found to be persuasive. As indicated in the previous office action, the specification at pages 29-30 provides some explanation of the 'second drug substance' intended by the claim, however, the scope of the claim includes therapeutic agents that are known and those that may be discovered in future, for which there is no enablement. Further, the entire scope of the therapeutic activity intended for the compounds of the invention is not enabled for the reasons provided previously.

Next applicant argues that 'claims 8-9 have been amended to recite specific diseases and cancel "preventing" language'. This amendment itself does not overcome the rejection. As indicated previously, the instant claims include method of treating a large list of diverse diseases, some of which are recited in the claims - acute or chronic rejection of organ or tissue, atherosclerosis, vascular occlusion, restenosis, hypertension, heart failure, chronic obstructive pulmonary disease, CNS disease, cancer, infectious disease, inflammatory disease, autoimmune disease. The difficulties associated with the treatment of some of the diseases encompassed by the claims were clearly established in the previous office action, some of the reasons are discussed here below.

The claims continue to encompass 'a method of treating **all** types of **cancer**' and the examiner has provided both reasoning including the nature of the invention, which is directed to an unpredictable art, citation of case law as well as relevant publication to support the reason for the rejection in the previous office action. Applicant has not identified any state of the art references that clearly establish correlation between the assays employed in the specification and clinical efficacy for the treatment of the claimed methods of treatment, which includes a method

of treatment of cancer generally. Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied on are reasonably predictive of *in vivo* efficacy by those skilled in the art.

The experimental procedure provided in the specification, pages 21-25 are related to the biological activity with respect to specific types (SYK and ZAP-70) of kinase inhibition. There is nothing in the specification how this data extrapolates to all the other types of diseases encompassed by the instant claims. Applicant did not state on record or provide any guidance that the assays provided are correlated to the clinical efficacy of the treatment of various disorders encompassed by the claims. As can be seen from specification, the *in vitro* data holds significant role in determining the dosage regimen based on the minimal effective concentration of each of the compound to achieve the desired inhibition of the enzymes.

The state of the art does not establish that a single therapeutic approach exists for the treatment of the types of cancers. The development of the most efficacious strategy for the treatment of cancers is based on understanding the underlying mechanisms of carcinogenesis. This includes the knowledge that the carcinogenic process is a multi-step, multi-mechanism process and that no two cancers are alike, in spite of some apparent universal characteristics, such as their inability to have growth control, to terminally differentiate, to apoptose abnormally and to have an apparent extended or immortalized life span. Since tumor promotion phase involves multiple mechanisms, there is no existence of a single therapeutic approach. The evidence of record does not disclose any known compounds of similar structure, which have been demonstrated to treat all cancers.

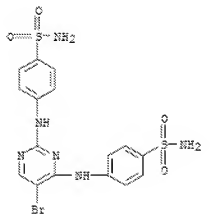
Applicant did not provide any explanation as to how treatment of <u>all</u> types of "acute or

chronic rejection of organ or tissue, atherosclerosis, vascular occlusion, restenosis, hypertension, heart failure, chronic obstructive pulmonary disease, CNS disease, cancer, infectious disease, inflammatory disease, autoimmune disease" is enabled based on the disclosed *in vitro* kinase activity. Applicant has not provided sufficient evidence that establishes that the disclosure would have enabled for one skilled in the art at the time of filing. The state of the art does not identify a single class of compounds that can treat all types of diseases in a patient or possess the biological activity of the instant claims. Further, one skilled in the art recognizes that there are complex interactions between individual genetic, developmental state, sex, dietary, environmental, drug, and lifestyle factors that contribute to various disease states, making it even more challenging to have a single therapeutic agent for the treatment of diverse diseases such as CNS diseases, cancer, infectious diseases, etc. of the instant claims. Rigorously planned and executed clinical trials, incorporating measurement of appropriate biomarkers and pharmacodynamic endpoints are critical for selecting the optimal dose and schedule for treatment of any particular disease. A detailed understanding of the molecular mode of action of the ischemic event alongside the elucidation of the molecular pathology of individual disease is required to identify the disease symptoms and individual patients that may benefit most from treatment. It is also important to construct a pharmacologic audit trail linking molecular biomarkers and pharmacokinetic and pharmacodynamic parameters for each individual disease therapeutic intervention. Therefore, it is maintained that applicants have not provided sufficient test assays or data to support the claimed compositions for the use of therapeutic methods commensurate in scope of the claims, as of the filing date of the application.

2. Claims 1-2, 4 and 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Pease et al., WO 01/64654. The reasons provided in the previous office action are incorporated here by reference.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant argues that 'the reference teaches a structure which carries a sulfonamide group on the different phenyl ring in a compound of formula (I), i.e., on the phenyl ring which carries R^7, R^8 and R^9 of the instant application and therefore, the reference does not teach a compound as recited in the instant amendment'. Contrary to applicant's arguments, the reference in fact teaches a compound that falls within the genus of the instant claims, see compound of Example 29 on page 40 (structure depicted below for convenience):

2,4-Di-(4-sulphamoylanilino)-5-bromopyrimidine



As can be seen from the above structure, the reference compound contains a sulfonamide group on the phenyl ring which carries R^1, R^2, R^3 of instant claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Deepak Rao/
Primary Examiner
Art Unit 1624

December 16, 2008